Research Article

Prevalence of metabolic syndrome in veterans with spinal cord injury

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Context/Objective: Recent literature would suggest the prevalence of metabolic syndrome in persons with spinal cord injury (SCI) is higher than that of the general population, although no large cohorts have yet been reported. Part of the controversy relates to the differing definitions provided for metabolic syndrome and the characterization of obesity in persons with SCI.

Design/Participants: The current retrospective investigation represents a cross-sectional cohort of 473 veterans with SCI from a single center in the mid-Atlantic region of the United States for whom modified International Diabetes Federation (IDF) criterion variables for the metabolic syndrome were available in the computerized personal record system (CPRS).

Outcome Measures: These variables included a surrogate marker of obesity appropriate to SCI (Body Mass Index (BMI) $\geq$ 22 kg/m^2), as well as indicators of diabetes, dyslipidemia and hypertension.

Results: Over 57% of the veterans assessed were determined to have metabolic syndrome by modified IDF criteria, including 76.7% with BMI $\geq$ 22 kg/m^2, 55.1% with or under treatment for hypertension, 49.7% with or previously diagnosed with diabetes mellitus, and 69.7% with or under treatment for high density lipoprotein (HDL) cholesterol under 40 mg/dl.

Conclusion: Metabolic syndrome and its constituent components appear to be more prevalent in veterans with SCI than in the general population, suggesting a greater need for identification and treatment interventions in this specialty population.

Keywords: Spinal cord injury, Obesity, Metabolic syndrome

Introduction

Adipose tissue has recently been demonstrated to secrete a number of hormones, proinflammatory adipokines, and prothrombotic agents that directly mediate metabolic syndrome and its associated morbidities.[1–3] The three most commonly used definitions for reporting and comparison of the metabolic syndrome have been drafted by the National Cholesterol Education Project Adult Treatment Panel III (NCEP ATP III), the World Health Organization (WHO) and the International Diabetes Federation (IDF). In 1998, the WHO definition of the metabolic syndrome focused on the central role of diabetes mellitus, plus at least two of the following: obesity (BMI > 30 kg/m^2 or Waist-to-hip ratio > 1), dyslipidemia (Triglycerides (TG) $\geq$ 150 mg/dl &/or HDL < 35 mg/dl in men or <39 mg/dl in women), hypertension (blood pressure (BP) $\geq$ 140/90 mm Hg), and microalbuminuria.[4] The third adult treatment panel of the National Cholesterol Education Project (ATP III) definition of the metabolic syndrome placed equal emphasis on any three of the following: obesity (waist circumference 102 $\geq$ cm in men, or $\geq$ 88 cm in women), dyslipidemia (TG $\geq$ 150 mg/dl &/or HDL < 40 mg/dl in men, < 50 mg/dl in women), hypertension (BP $\geq$ 130/85 mm Hg), and fasting glucose > 110 mg/dl.[5] Most recently, the International Diabetes Federation (IDF) definition of metabolic syndrome has emphasized the role of central obesity (waist circumference $\geq$ 94 cm in men, $\geq$ 80 cm in women) plus any two of the following: dyslipidemia (TG $\geq$ 150 mg/dl or on treatment; HDL < 40 mg/dl

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DOI 10.1080/10790268.2017.1423266

for men, < 50 mg/dl for women or on HDL treatment), hypertension (≥ 130 mm Hg systolic or ≥ 85 mm Hg diastolic, or on treatment for hypertension), fasting glucose ≥ 100 mg/dl or previously diagnosed with type 2 diabetes mellitus.[6] All three definitions continued to be used in current literature, but the authors have elected to focus on the definition provided by the IDF since it seems to reflect the clinical role of central adiposity and its impact on adiposity-related comorbidities.

Utilizing these definitions for metabolic syndrome in persons with spinal cord injury (SCI) whose blood pressure abnormalities could be confounded by neurogenic hypotension, and whose waist circumferences may be expanded due to abdominal muscle paralysis may be inappropriate. Nonetheless, recent reports have demonstrated unexpected hypertension in veterans with SCI,[7] and evidence from our laboratory has suggested that obesity is more prevalent after SCI than in the general population, which would appear to put those with SCI at increased risk for metabolic syndrome.[8,9] The pathophysiological consequences of obesity within a given individual with SCI are subject to that person's genetic sensitivity to endogenous adipokines and hormones, as well as the volume of adipose tissue secreting these agents.[10]

Surprising to the authors, the Agency for Healthcare Research and Quality (AHRQ) recently reported that "the existing evidence does not indicate that adults with SCI are at markedly greater risk for carbohydrate and lipid disorders or subsequent cardiovascular sequelae than able-bodied adults."[11] The report was limited to epidemiological investigations reported after 1990 with at least 100 subjects and to interventional studies from 1996-2007. Moreover, the report acknowledges that the evidence is limited by relatively few studies, small sample sizes, lack of appropriate control groups, failure to adjust for known confounding variables, and variations in reported outcomes.

Unfortunately, traditional measures of obesity, including BMI or waist circumference, have not been appropriately validated in persons with SCI, whose adiposity appears significantly elevated when compared to able-bodied individuals of similar age, weight and sex. In fact, the standard application of BMI grossly underestimates obesity in persons with SCI, as demonstrated in a recent, comprehensive review.[12] Further, waist circumferences are not typically recorded in the VHA computerized personal record system (CPRS), whereas heights and weights have been recorded for years, so that BMI is the closest surrogate measure of obesity available for review. The aims of the current study were to (a) to determine the prevalence of obesity in SCI veterans using the standard definition of BMI ≥ 30 kg/m^2 and the proposed SCI-appropriate definition of BMI ≥ 22 kg/m^2 as a surrogate for obesity instead of waist circumference, (b) to determine the prevalence of Metabolic Syndrome in veterans with SCI using both the standard and proposed SCI-appropriate definitions of BMI, and (c) to examine the associations between obesity and each of the other Metabolic Syndrome risk factors (hypertension, diabetes, increased triglycerides, reduced HDL) in veterans with SCI using both obesity definitions.

Methods

The plan for retrospective analysis was reviewed and approved by the Institutional Review Board and Research and Development committees at the Hunter Holmes McGuire Veterans Medical Center (HHMVAMC) prior to implementation. Of the 1,568 veterans listed in the national VHA Spinal Cord Injury & Disorders (SCI&D) registry for the HHMVAMC catchment area, 669 had recently (within the past 5 years) been admitted to the SCI&D Center. The VHA computerized personal record system (CPRS) was used to validate that all veterans had SCI between C2 and S5, and a de-identified database was created for evaluation. The variables analyzed for Metabolic Syndrome were modified from the 2005 IDF guidelines; because waist circumferences were not routinely available in CPRS, the WHO definition of BMI ≥ 30 kg/m^2 or SCI-corrected BMI ≥ 22 kg/m^2 were used as substitute markers for central obesity as has recently been suggested.[13,14]

Variables

Demographic variables available for analysis included age, sex, and race. Age was measured in years and race was categorized as Caucasian, African American, or Other. Injury characteristics available for analysis included level of injury, American Spinal Injury Association (ASIA) impairment scale (AIS), and time since injury. Level of injury was measured at the most recent visit and was classified as tetraplegia, high paraplegia (T1-T6), or low paraplegia (below T6). AIS level of impairment (A, B, C, D, E) was measured at the most recent visit and was re-classified as A, B, C, or D/E, and time since injury was classified as less than 10 years, 10 to 30 years, or more than 30 years. Participant height (cm), weight (kg), and body mass index (kg/m^2), along with the metabolic characteristics of fasting blood glucose (mg/dl), low density lipoproteins (mg/dl), high density lipoproteins (mg/dl), triglycerides (mg/dl), and systolic and diastolic blood pressure (SBP and DBP, mmHg) were available for analysis. Additionally,

variables pertaining to previous diagnosis of diabetes (yes or no), treatment for elevated triglycerides (yes or no), treatment for reduced HDL (yes or no) and treatment for hypertension (yes or no) were recorded.

Statistical methods

All statistical analyses were performed using R (R Foundation for Statistical Computing, Vienna, Austria). Demographic characteristics, injury characteristics, and metabolic measures were described using mean and standard deviations (SD) or medians and interquartile ranges (IQR) for continuous variables, and counts and percentages for categorical variables.

The prevalence of each Metabolic Syndrome factor (hypertension, diabetes, elevated triglycerides, and reduced HDL) was estimated using a 95% confidence interval. Additionally, 95% confidence intervals were used to estimate the prevalence of obesity defined as BMI $\geq 30\ kg/m^2$ or the prevalence of obesity defined as BMI $\geq 22\ kg/m^2$. Similarly, 95% CI's were used to estimate the prevalence of metabolic syndrome using each definition of obesity.

Simple logistic regression models were fit to assess the univariate relationships between obesity and each of the other metabolic syndrome factors using both definitions of obesity. Multiple logistic regression models were fit using both obesity definitions to estimate the odds of obesity for each metabolic syndrome factor, adjusting for age, race, level of injury, and ASIA Impairment Scale (AIS). Sex was not considered as a controlling variable since there were only 7 female participants. For the unadjusted (simple logistic regression) and adjusted (multiple logistic regression) models, the odds ratio comparing the odds of having each non-obesity Metabolic Syndrome risk factor, for those who were defined as obese versus those who were not defined as obese, was estimated along with 95% confidence intervals.

Table 1 Continuous demographic and metabolic characteristics for participants.

	N	Mean (median)	SD (IQR)
Demographic Characteristics			
Age	473	56.0	13.1
Time since injury (years)*	473	(19.2)	(9.4 to 31.0)
Metabolic characteristics			
BMI (kg/m^2)	473	25.9	6.3
Weight (kg)	473	83.9	20.1
Height (cm)	472	180.0	8.0
Fasting glucose (mg/dl)*	473	(98.0)	(87.0 to 118.0)
LDL (mg/dl)	464	99.0	31.9
HDL (mg/dl)*	468	(35.7)	(29.9 to 45.2)
Triglycerides mg/dl*	469	(106.0)	(76.0 to 152.0)
SBP (mmHg)	473	125.0	22.3
DBP (mmHg)	473	70.0	13.6

SD, Standard deviation; IQR, Interquartile range.
*Medians and IQRs reported rather than means and SD for skewed variables.

Results

Description of the sample

The demographic, injury, and metabolic characteristics of the sample are summarized in Tables 1 and 2. Participants were primarily male (98.5%) and Caucasian (55.4%). The average age at the time of the study was 56.0 (SD = 13.1) years and the median time since injury was 230.4 months (19.2 years). With respect to the injury characteristics, nearly half of the eligible participants were classified as AIS A (45.9%) and/or had tetraplegia (49.6%).

Prevalence of obesity in veterans with SCI using standard and proposed SCI-appropriate definitions of obesity (Aim 1)

Using the WHO standard of BMI ≥ 30 as the definition of obesity, 26.9% (95% CI = 22.9, 30.8) of participants

Table 2 Categorical demographic, injury, and metabolic characteristics for participants.

	N	Percent
Demographic characteristics		
Sex		
Male	466	98.5
Female	7	1.5
Race		
White	262	55.4
African American	160	33.8
Other	51	10.8
Injury characteristics		
Level of Injury		
Tetraplegia	234	49.6
High (T1-T6) paraplegia	84	17.8
Low (below T6) paraplegia	154	32.6
AIS		
A complete	217	45.9
B	71	15.0
C	65	13.7
D or E	120	25.4
Time since injury		
$\leq$ 10 years	121	25.7
10 to 30 years	223	47.3
$\geq$ 30 years	127	27.0
Metabolic factors		
Hypertension		
No	212	44.8
Yes	261	55.2
Diabetes		
No	238	50.3
Yes	235	49.7
Raised triglycerides		
No	295	62.9
Yes	174	37.1
Reduced HDL		
No	142	30.3
Yes	326	69.7

Table 3 Prevalence of metabolic syndrome and individual metabolic syndrome risk factors.

	Prevalence (%)			
	N	Estimate	SE	95% CI
Obesity (BMI ≥ 30)	473	26.9	0.020	(22.9, 30.8)
Obesity (BMI ≥ 22)	473	76.7	0.019	(72.9, 80.6)
Hypertension	473	55.1	0.023	(50.6, 59.5)
Diabetes	473	49.8	0.023	(45.3, 54.3)
Raised triglycerides	470	37.2	0.022	(32.9, 41.6)
Reduced HDL	469	69.7	0.021	(65.6, 73.9)
Metabolic syndrome (BMI ≥ 30)	471	22.9	0.019	(19.1, 26.7)
Metabolic syndrome (BMI ≥ 22)	468	57.5	0.023	(53.1, 62.0)

were classified as obese. After reducing the BMI threshold of obesity from 30 to 22 as suggested in recent literature,[13,14] the prevalence of obesity in the sample increased to 76.7% (95% CI = 72.9, 80.6); see Table 3.

Prevalence of Metabolic Syndrome in veterans with SCI using standard and proposed SCI-appropriate definitions of obesity (Aim 2)

The prevalence of Metabolic Syndrome and each Metabolic Syndrome factor is described in Table 3. Hypertension was present in 55.1% (95% CI = 50.6, 59.5) of participants and 49.8% (95% CI = 45.3, 54.3) of participants were diabetic. Additionally, dyslipidemia was notable, as 37.2% (95% CI = 32.9, 41.6) of participants had elevated triglycerides and 67.9% (95% CI = 65.6, 73.9) of participants had reduced HDL.

Using BMI ≥ 30 as the definition of obesity, metabolic syndrome was found in 22.9% (95% CI = 19.1, 26.7) of participants. After decreasing the BMI threshold of obesity from 30 kg/m^2 to the SCI-appropriate definition of 22 kg/m^2, the prevalence of metabolic syndrome increased to 57.5% (95% CI = 53.1, 62.0).

Association between obesity and each factor of Metabolic Syndrome using standard and proposed SCI-appropriate definitions of obesity (Aim 3)

A summary of the prevalence of Metabolic Syndrome factors by obesity, for both definitions of obesity, is shown in Table 4. For example, using BMI ≥ 30 as the definition of obesity, we see that 67.1% of obese subjects were hypertensive, while 59.8% of obese subjects were hypertensive when obesity is defined as BMI ≥ 22. The unadjusted and adjusted relationship between each definition of obesity and the non-obesity Metabolic Syndrome risk factors are summarized in Table 5. Without adjusting for any injury or patient characteristics, there was a significant relationship between hypertension and obesity, using both obesity definitions (BMI ≥ 22 kg/m^2, $P < 0.001$; BMI ≥ 30 kg/m^2, $P = 0.004$) with the odds of hypertension significantly greater for obese patients as compared to non-obese patients. More specifically, the odds of hypertension for obese patients were 2.22 and 1.86 times greater than the odds of hypertension for non-obese patients using obesity definitions of using BMI ≥ 22 kg/m^2 and BMI ≥ 30 kg/m^2 as the definitions of obesity, respectfully.

Similarly without adjusting for injury or patient characteristics, there was a significant relationship between diabetes and obesity using both obesity definitions (BMI ≥ 22 kg/m^2, $P = 0.003$; BMI ≥ 30 kg/m^2, $P < 0.001$) with the odds of diabetes significantly greater for obese individuals regardless of BMI threshold. The odds of diabetes were 1.93 and 2.09 times greater for obese patients than the odds of diabetes for non-obese patients using BMI ≥ 22 kg/m^2 and BMI ≥ 30 kg/m^2 as the definition of obesity, respectfully.

The unadjusted relationship between elevated triglycerides and obesity was also significant for both

Table 4 Distribution of metabolic syndrome factors by obesity status and definitions of obesity.

	Obesity (BMI ≥ 30)				Obesity (BMI ≥ 22)			
	No (N = 346)		Yes (N = 127)		No (N = 110)		Yes (N = 363)	
Metabolic syndrome factor	N	Percent	N	Percent	N	Percent	N	Percent
Hypertension								
No	169	48.8	43	33.9	66	60.0	146	40.2
Yes	177	51.2	84	67.1	44	40.0	217	59.8
Diabetes								
No	191	55.2	47	37.0	69	62.7	169	46.6
Yes	155	44.8	80	63.0	41	37.3	194	53.4
Raised triglycerides								
No	232	67.4	63	50.4	81	73.6	214	59.6
Yes	112	32.6	62	49.6	29	26.4	145	40.4
Reduced HDL								
No	118	34.4	24	19.2	43	39.1	99	27.7
Yes	225	65.6	101	80.8	67	60.9	259	72.3

definitions of obesity (BMI $\geq 22\ kg/m^2$, $P = 0.007$; BMI $\geq 30\ kg/m^2$, $P = 0.001$). The odds of elevated triglycerides were 1.88 and 2.03 times greater for obese patients as compared to non-obese patients for BMI $\geq 22\ kg/m^2$ and BMI $\geq 30\ kg/m^2$ as the definitions of obesity, respectfully.

Finally, the unadjusted odds of low HDL were significantly greater for obese patients regardless of the definition of obesity (BMI $\geq 22\ kg/m^2$, $P = 0.001$; BMI $\geq 30\ kg/m^2$, $P = 0.025$). The odds of low HDL were 1.68 and 2.19 times greater for obese patients as compared to non-obese patients using BMI $\geq 22\ kg/m^2$ and BMI $\geq 30\ kg/m^2$ as the definitions of obesity, respectfully.

After controlling for patient characteristics (age, race, level of injury, and ASIA level of impairment), the odds of diabetes, high triglycerides, and low HDL are significantly greater for obese individuals as compared to non-obese individuals regardless of the definition of obesity. Odds ratios that changed by more than 10% after controlling for patient characteristics included reduced HDL using both definitions of obesity. This relatively large change is indicative of the mediating effects the patient characteristics have on the relationship between obesity and the Metabolic Syndrome risk factors.

Discussion

Since the AHRQ report on carbohydrate and lipid disorders in SCI came out, several reports[15–18] have attempted to address the prevalence of metabolic syndrome in this population, but none to date have included such a robust sample size as reported here. Of particular note, the current data provide a comparison of the WHO definition of obesity (BMI $> 30\ kg/m^2$) and the SCI-appropriate definition of obesity (BMI $\geq 22\ kg/m^2$) with profound impact on the apparent prevalence of metabolic syndrome in veterans with SCI. This distinction is critical, since BMI fails to distinguish body composition differences in persons with SCI who have significantly reduced bone mass and sarcopenia due to paralysis, such that a greater percentage of their body weight is comprised of adipose tissue which appears to be the key driver of the metabolic syndrome.[8] Some recent investigations have suggested waist circumference in persons with SCI is a better indicator of obesity than is BMI;[19,20] however, those studies have not been validated against the current gold standard of obesity assessment, i.e., the 4-compartment model. Regardless, waist circumferences were not available for use in the current study as described above. While validation of assessment techniques in body composition are currently underway in our laboratory, several studies indicate that for persons with SCI, even BMI $> 22\ kg/m^2$ is associated with percent body fat (%BF) considered obese by standard definitions.[9,13,14] Hence, the 57.5% prevalence of metabolic syndrome in SCI associated with BMI $\geq 22\ kg/m^2$ in the present study remains conservative, and likely underestimates true prevalence in this high risk population.

Our results are fairly different from those of Maruyama *et al.*[15] who reported that 43% of 44 persons with SCI had metabolic syndrome as defined by ATP III. Of note, the ATP III criteria include fasting glucose $> 110\ mg/dl$, as opposed to the $100\ mg/dl$ cut-off provided in the IDF criteria, suggesting that the prevalence may have been higher using the modified IDF definition. Furthermore, differences in sample size between Maruyama *et al.*[15] and the present study could account for the variation in the reported prevalence of metabolic syndrome. Nash *et al.*[16] also used the ATP III definition of metabolic syndrome and reported 34% prevalence of metabolic syndrome among $n = 41$ paraplegics with SCI. The latter study did not include persons with tetraplegia who are likely more obese and at higher risk more metabolic syndrome than those with paraplegia due to greater relative sarcopenia, sympathetic blunting, and lower metabolic rates. A follow up study a few years later, however, demonstrated cardiometabolic dysfunction prevalence with SCI-specific cutoff BMI $\geq 22\ kg/m^2$ and found that doing so increased the range from 27-36% to 82-85% prevalence.[18]

Because of our choice to conservatively assign obesity at BMI $\geq 22\ kg/m^2$ in this sample, the prevalence of obesity reported as 76.7% in all likelihood underestimates the true obesity prevalence in our SCI veteran population. We had previously reported BMI $> 25\ kg/m^2$ in 53% of 7,959 veterans with SCI such that the conservative estimate is consistent with current literature.[7] However, BMI of approximately $25\ kg/m^2$ in individuals with SCI has been demonstrated by several body composition assessment techniques to correlate with %BF $> 33\%$, which is well above the 25% BF threshold for obesity accepted by the exercise science community.[9,12,21–25] High body fat relative to fat-free body mass in SCI is especially important in the development of metabolic syndrome, since adipose tissue directly and indirectly increases glucose intolerance, dyslipidemia and hypertension.[2,8]

Adipose tissue increases the accumulation of ceramides, diacylglerol, and fatty acyl-Co-A within hepatocytes and myocytes, inhibiting the phosphatidylinositol 3-kinase (PI-3 kinase) cascade that is necessary for activation and translocation of GLUT4 receptors to

Table 5 Unadjusted and adjusted odds ratios of metabolic syndrome factors for obese versus non-obese by definition of obesity.

	Unadjusted					Adjusted				
	Obesity (BMI ≥ 30) yes vs. no									
Metabolic syndrome factor	χ^2_1	P-value	OR	95% CI		χ^2_1	P-value	OR	95% CI	
Hypertension	8.32	0.004	1.86	(1.22, 2.86)	†	4.23	0.04	1.61	(1.24, 3.12)	†
Diabetes	12.07	< 0.001	2.09	(1.38, 3.20)	†	11.87	0.001	2.18	(1.22, 3.03)	†
Raised triglycerides	11.21	0.001	2.03	(1.34, 3.09)	†	11.80	0.001	2.19	(1.12, 3.02)	†
Reduced HDL	9.72	0.001	2.19	(1.35, 3.68)	†	14.35	< 0.001	2.78	(1.21, 3.12)	†
	Obesity (BMI ≥ 22) yes vs. no									
Hypertension	13.03	< 0.001	2.22	(1.44, 3.46)	†	8.24	0.004	1.96	(1.03, 2.55)	†
Diabetes	8.68	0.003	1.93	(1.25, 3.01)	†	7.77	0.005	1.91	(1.40, 3.41)	†
High triglycerides	6.97	0.007	1.88	(1.18, 3.07)	†	5.71	0.017	1.82	(1.40, 3.43)	†
Reduced HDL	5.15	0.025	1.68	(1.07, 2.62)	†	7.72	0.005	1.94	(1.66, 4.81)	†

† Indicates significance ($\alpha = 0.05$); BMI, body mass index; HDL, high-density lipoprotein; OR, odds ratio; CI, confidence interval.

facilitate glucose transport within the cell.[26] Our reported prevalence of glucose intolerance in 50.3% of this sample is consistent with previous reports in the literature, including a small sample of tetraplegics and paraplegics among whom 62% and 50% had abnormal glucose tolerance tests, respectively.[27] Similarly, earlier reports suggested 50% of persons with SCI screened with oral glucose tolerance tests were found to have impaired glucose tolerance.[28] Unfortunately, those previous investigations did not capture information related to body composition or adiposity. Since fasting glucose does not always correlate with glucose intolerance in persons with SCI, our current prevalence report of glucose abnormalities may likely underestimate the true prevalence.[29]

Excess adipose tissue increases the hepatic circulation of non-esterified fatty acids which subsequently increase hepatic LDL production and decrease HDL production, significantly worsening the ratio of cholesterol to HDL and increasing one's risk for atherosclerosis and endothelial dysfunction.[2,8] Additionally, recent literature has documented a high prevalence (49%) of non-alcoholic fatty liver disease in individuals with chronic SCI.[30] The prevalence of dyslipidemia was 70.6% in the current cohort, which is fairly similar to recent reports with much smaller cohorts.[16,18,29] Moreover, we have previously demonstrated strong relationships between both visceral and subcutaneous abdominal fat and dyslipidemia in persons with SCI.[31]

The prevalence of hypertension in our cohort with BMI $\geq$ 22 kg/m^2 (56.7%) was somewhat higher than reported in previous SCI literature,[7,18] and may reflect an older, more obese population, as well as slightly stricter guidelines by IDF criteria. Of note, only baseline blood pressures were reported for those individuals who might be at risk for autonomic dysreflexia (AD) to ensure the prevalence truly reflected hypertension rather than episodic AD. Further, since persons with SCI are often diagnosed with neurogenic hypotension early in their injury, these findings warrant additional concern for the impact of cumulative adipose tissue on blood pressure dynamics. Adiposity contributes to hypertension through the chronic effect of proinflammatory adipokine on arterial endothelium, increased sympathetic nervous system activity due to leptin produced by adipocytes, angiotensinogen released from fat cells and mechanic compression by visceral fat on the kidneys with increased intrarenal pressures and subsequent sodium retention.[2,8]

We acknowledge of number of limitations to the current study, including the limited number of veterans meeting eligibility criteria due to missing data. Using a surrogate marker for obesity of BMI $\geq$ 22 kg/m^2 may raise concerns among those unfamiliar with body composition after SCI about overestimating its prevalence, particularly since it was not the parameter for obesity endorsed by the IDF. However, a BMI $\geq$ 22 kg/m^2 is a very conservative threshold when compared to body fat estimates exceeding 25% (i.e., obese).[9,12] Nonetheless, we have provided prevalence data in Table 4 for metabolic syndrome constituents based on SCI-adjusted BMI (22 kg/m^2) as well as non-SCI BMI criteria (30 kg/m^2) in order to allow side-to-side comparisons of the relative impact. Finally, we recognize that adiposity is not the sole contributor to the metabolic syndrome, and acknowledge that some veterans with BMI $<$ 30 kg/m^2 may not meet criteria, while a similar number may meet thresholds for diabetes, dyslipidemia and hypertension, yet be well under BMI $<$ 22 kg/m^2 based on genetic variability or other factors.

Conclusion

The current investigation represents a significant and essential contribution to the SCI literature, with the largest cohort yet reported on the prevalence of metabolic syndrome and its relative contributing factors. Over 57% of the veterans assessed were determined to have metabolic syndrome by modified IDF criteria (using BMI $\geq$ 22 kg/m^2 as a surrogate for obesity), including 76.7% with BMI $\geq$ 22 kg/m^2, 55.1% with or under treatment for hypertension, 49.7% with or previously diagnosed with diabetes mellitus, and 69.7% with HDL-cholesterol under 40 mg/dl. Future research is needed to determine the true prevalence of obesity in this population using 4-compartment modeling or appropriately validated body composition techniques to assess relative and absolute body fat, since BMI clearly underestimates obesity in this special population. Additionally, the relationship between fat mass and constituent factors of the metabolic syndrome needs to be further elucidated with relevant biomarkers associated with the known pathophysiology. We recently demonstrated that systemic inflammation present after SCI is highly associated with adiposity, implicating proinflammatory adipokines as the primary mediators of the metabolic syndrome in persons with SCI.[3] Finally, appropriate and realistic intervention strategies need to be determined in order to promote long-term health and wellness in our veterans with SCI.

Disclaimer statements

Contributors None.

Funding This work was conducted at the Hunter Holmes McGuire VAMC, Richmond, VA.

Conflicts of interest The authors certify that they have no financial or other conflicts of interest.

Ethics approval None.

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